

FIG. 1A

pET22b(+) forward primer:

5'-CGGGATCCT TCT GTT GAT CAC GGC TTC-3' (SEQ ID NO:3)

pET22b(+) reverse primer:

5'-CCCAAGCTT TGT TCT TCT CAT ACA GAC-3' (SEQ ID NO:4)

pPICZαA forward primer:

5'-TCGGAATTTC TCT GTT GAT CAC GGC TTC-3' (SEQ ID NO:15)

pPICZαA reverse primer:

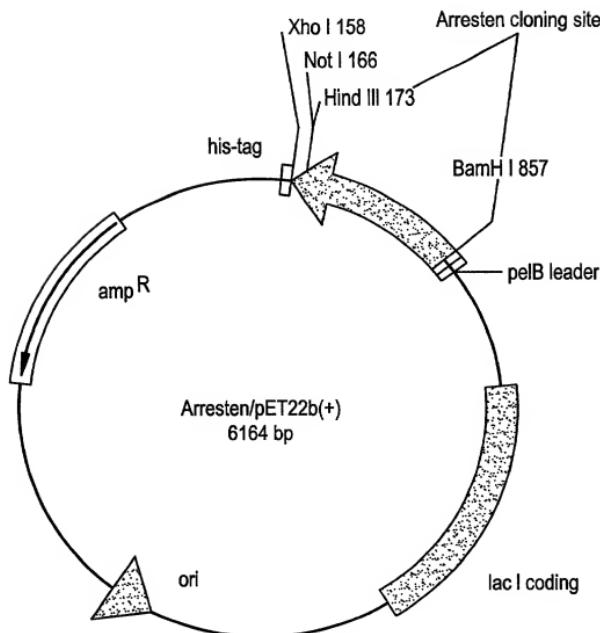
5'-TGCTCTAGAGG TGT TCT TCT CAT ACA GAC TTG GCA-3' (SEQ ID NO:16)

5	10	15	20	25	30	35	40	45																																																																																																																																		
<u>tct</u>	<u>gtt</u>	<u>gat</u>	<u>cac</u>	<u>ggc</u>	<u>ttc</u>	ctt	gtg	acc	agg	cat	agt	caa	aca	ata																																																																																																																												
50	55	60	65	70	75	80	85	90	95	100	105	110	115	120	125	130	135																																																																																																																									
gat	gac	cca	cag	tgt	cct	tct	ggg	acc	aaa	att	ctt	tac	cac	ggg	tac	tct	ttg	ctc	tac	gtg	caa	ggc	aat	gaa	cgg	gcc	cat	gga	cag																																																																																																													
140	145	150	155	160	165	170	175	180	185	190	195	200	205	210	215	220	225	gac	ttg	ggc	acg	gcc	ggc	agc	tgc	ctg	cgc	aag	ttc	agc	aca	atg	ccc	ttc	ctg	tcc	tgc	aat	att	aac	aac	gtg	tgc	aac	ttt	gca	tca																																																																																											
230	235	240	245	250	255	260	265	270	275	280	285	290	295	300	305	310	315	cga	aat	gac	tac	tcg	tac	tgg	ctg	tcc	acc	cct	gag	ccc	atg	ccc	atg	tca	atg	tcg	atg	gca	ccc	atc	acg	ggg	aaa	ata	aga	cca	ttt	att																																																																																										
320	325	330	335	340	345	350	355	360	365	370	375	380	385	390	395	400	405	cac	agc	cag	acc	att	cag	atc	cca	ccg	tgc	ccc	agc	ggg	tgg	tcc	tcg	ctg	tgg	tac	ttt	gtc	tgt	gtt	gag	ggc	cct	gcc	atg	gtg	atg	gcc	gtg	atc	ttt	gtc	ccc	ccg	atc	ttt	gtc	tgt	gtt	gag	ggc	cct	gcc	atg	gtg	atg	gcc	gtg																																																																						
410	415	420	425	430	435	440	445	450	455	460	465	470	475	480	485	490	495	gca	gaa	ggc	tct	ggc	caa	gcc	ctg	gog	tcc	ccc	ggc	tcc	tgc	ctg	500	505	510	515	520	525	530	535	540	gag	gag	ttt	aga	agt	gct	cca	ttc	atc	gag	tgt	cac	ggc	cgt	ggg	545	550	555	560	565	570	575	580	585	acc	tgc	aat	tac	tac	gca	aac	gct	tac	agc	ttt	tgg	ctc	gcc	acc	590	595	600	605	610	615	620	625	630	ata	gag	agg	agc	gag	atg	ttc	aag	aag	cct	acg	ccg	tcc	acc	ttg	635	640	645	650	655	660	665	670	675	aag	gca	ggg	gag	ctg	cgc	acg	cac	gtc	agc	cgc	tgt	caa	gtc	tat	680	685	690	ata	gag	aga	aga	aca	taa	(SEQ ID NO:1)

FIG. 1B

5 10 15 20 25 30 35 40 45
SVD HGF LVT RHS QTI DDP QCP SGT KIL YHG YSL LYV QGN ERA HGQ
50 55 60 65 70 75 80 85 90
DLG TAG SCL RKF STM PFL FCN INN VCN FAS RND YSY WLS TPE PMP
95 100 105 110 115 120 125 130 135
MSM API TGE NIR PFI SRC AVC EAP AMV MAV HSQ TIQ IPP CPS GWS
140 145 150 155 160 165 170 175 180
SLW IGY SFV MHT SAG AEG SGQ ALA SPG SCL BEF RSA PFI ECH GRG
185 190 195 200 205 210 215 220 225
TCN YYA NAY SFW LAT IER SEM FKK PTP STL KAG ELR THV SRC QVC
229
MRR T (SEQ ID NO:2)

FIG. 2



Forward primer: 5'-cgggatccctctgtgatcacggcttc-3'

Reverse primer: 5'-ccaaagcttgcgtctctatacagac-3'

FIG. 3A

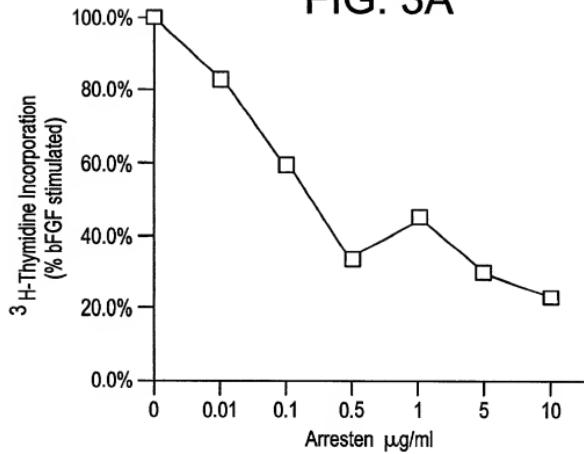


FIG. 3B

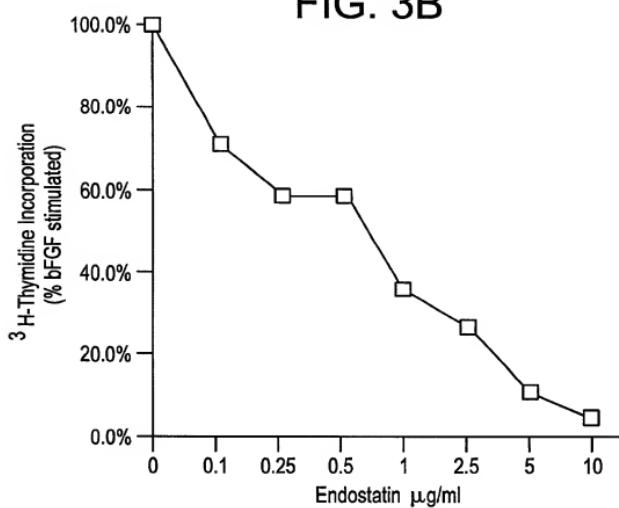


FIG. 4A

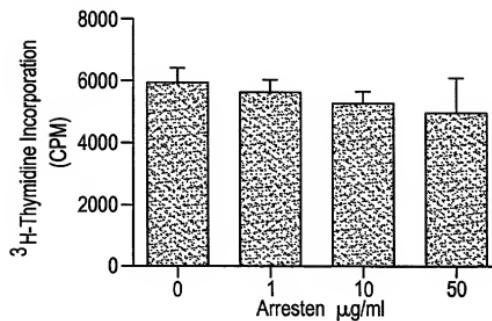


FIG. 4B

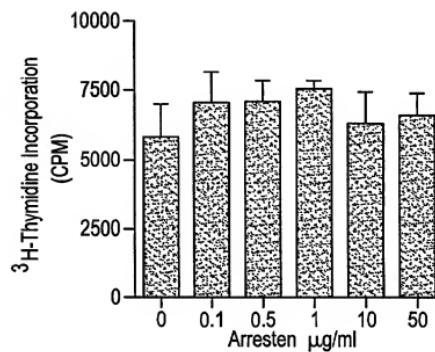


FIG. 4C

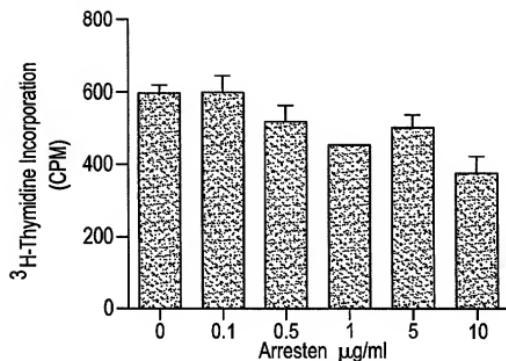
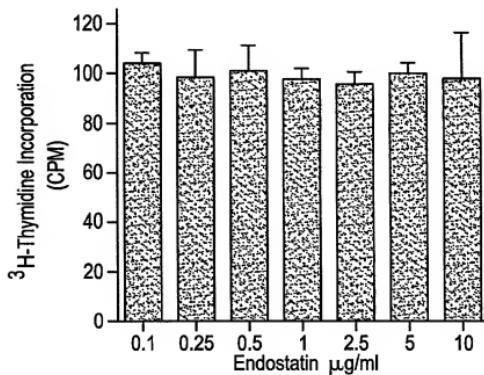


FIG. 4D



Docket No.: 1440.1027-016
Title: ANTI-ANGIOGENIC PROTEINS AND...
Inventors: Raghuram Kalluri

FIG. 5A

Control

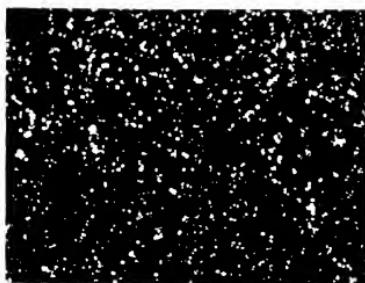


FIG. 5B

Arresten 2 µg/ml



FIG. 5C

Endostatin 20 µg/ml

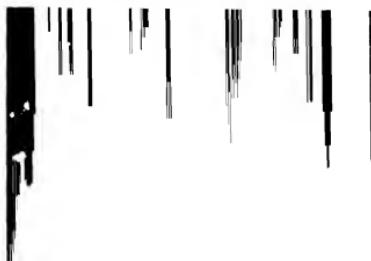


FIG. 6

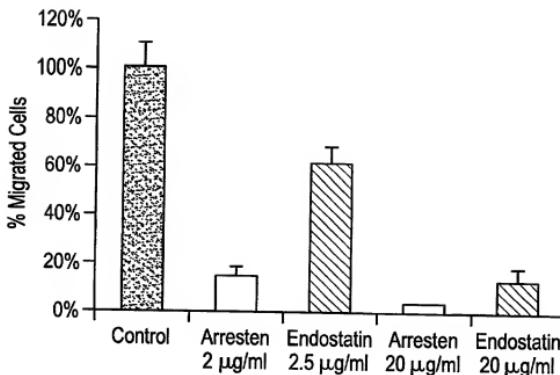


FIG. 7

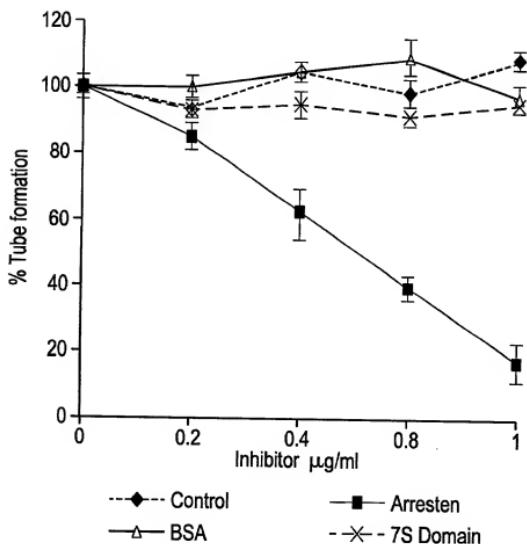


FIG. 8A

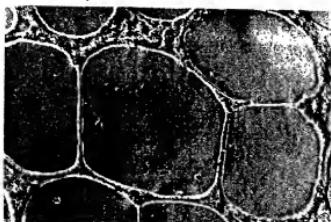


FIG. 8B

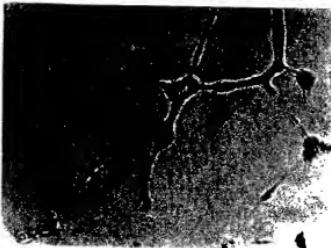


FIG. 9A

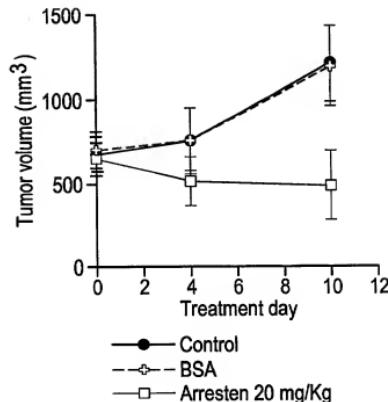


FIG. 9B

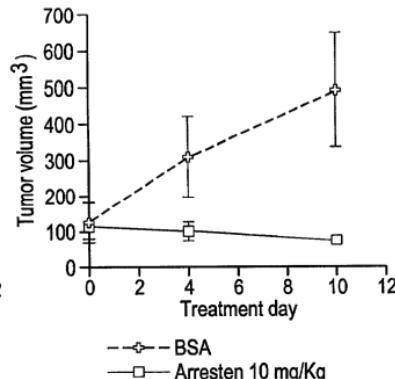


FIG. 9C

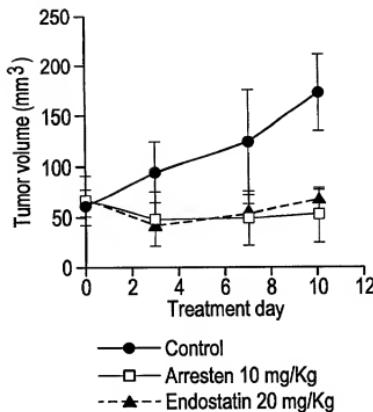
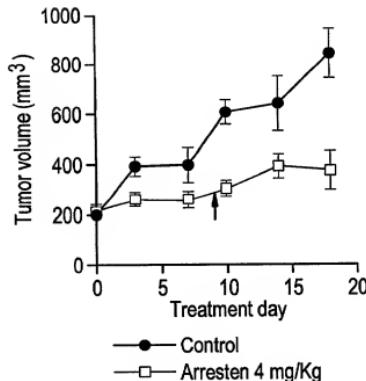


FIG. 9D



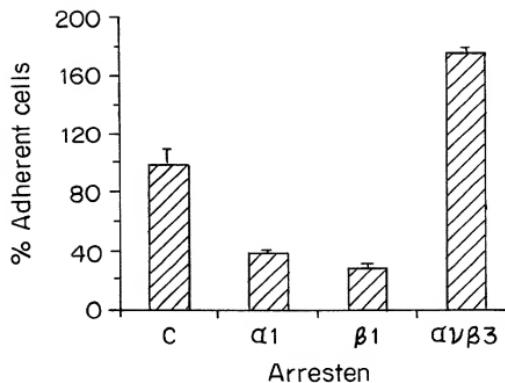


FIG. IOA

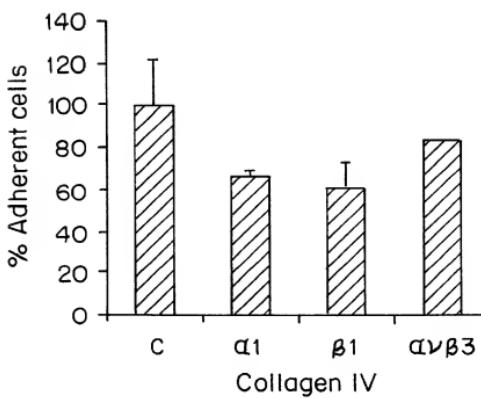


FIG. IOB

FIG. 11A

pET22b(+) forward primer:

5'-CGGGATCCT GTC AGC ATC GGC TAC CTC-3' (SEQ ID NO:7)

pET22b(+) reverse primer:

5'-CCCAAGCTT CAG GTT CTT CAT GCA CAC-3' (SEQ ID NO:8)

pPICZ α A forward primer:

5'-TTCCGAATTGTCAGCATCGCTACCTCCTG-3' (SEQ ID NO:17)

nPICZ α A reverse primer:

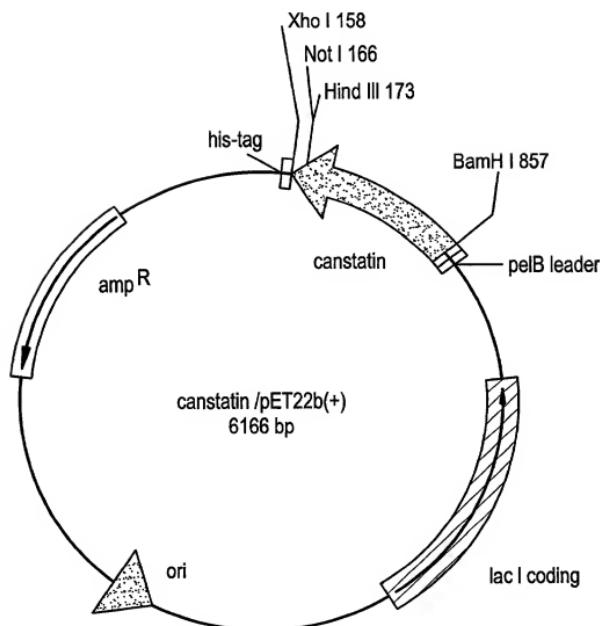
5'-GGGGTACCCC CAG GTT CTT CAT GCA CAC CTG G-3' (SEQ ID NO:18)

5	10	15	20	25	30	35	40	45
gtc	agc	atc	ggc	tac	ctc	ctg	gtg	aag
50	55	60	65	70	75	80	85	90
gag	ccc	atg	tgc	ccg	gtg	ggc	atg	aaa
95	100	105	110	115	120	125	130	135
agc	ctg	ctg	tac	ttc	gag	ggc	cag	cac
140	145	150	155	160	165	170	175	180
ctg	ggg	ctg	gcg	ggc	tcc	tgc	cgg	ttc
185	190	195	200	205	210	215	220	225
ttc	ctg	tac	tgc	aac	cct	ggt	gat	gtc
230	235	240	245	250	255	260	265	270
aat	gac	aag	tcc	tac	tgg	ctc	tct	acc
275	280	285	290	295	300	305	310	315
atg	ccc	gtg	gcc	gag	gac	gag	atc	aag
320	325	330	335	340	345	350	355	360
tct	gtg	tgt	gag	gcc	ccg	gcc	atc	gcc
365	370	375	380	385	390	395	400	405
aat	gtc	tcc	atc	cca	cac	tgc	cca	gtt
410	415	420	425	430	435	440	445	450
atc	gga	tat	tcc	ttc	ctc	atg	cac	acg
455	460	465	470	475	480	485	490	495
ggt	ggc	caa	tca	ctg	gtg	tca	ccg	ggc
500	505	510	515	520	525	530	535	540
cgc	gcc	aca	cca	ttc	atc	gaa	tgc	aat
545	550	555	560	565	570	575	580	585
cac	tac	tac	gcc	aac	aag	tac	agc	tcc
590	595	600	605	610	615	620	625	630
gag	cag	agc	ttc	cag	ggc	tgc	ccc	tcc
635	640	645	650	655	660	665	670	675
ggc	ctc	atc	cgc	aca	cac	atc	agc	cgc
680								
aac	ctg	tga		(SEQ ID NO:5)				

FIG. 11B

5 10 15 20 25 30 35 40 45
VSI GYL LVK HSQ TDQ EPM CPV GMN KLW SGY SLL YFE GQE KAH NQD
50 55 60 65 70 75 80 85 90
LGL AGS CLA RFS TMP FLY CNP GDV CYY ASR NDK SYW LST TAP LPM
95 100 105 110 115 120 125 130 135
MPV AED EIK PYI SRC SVC EAP AIA IAV HSQ DVS IPH CPA GWR SLW
140 145 150 155 160 165 170 175 180
1GY SFL MHT AAG DEG GGQ SLV SPG SCL EDF RAT PFI ECN GGR GTC
185 190 195 200 205 210 215 220 225
HYY ANK YSF WLT TIP EQS FQG SPS ADT LKA GLI RTH ISR CQV CMK
227
NL (SEQ ID NO:6)

FIG. 12



Forward primer: 5'-cgggatccgtcagcatcggttacctc-3'

Reverse primer: 5'-cccaaggcttcaggttttcatgcacac-3'

FIG. 13A

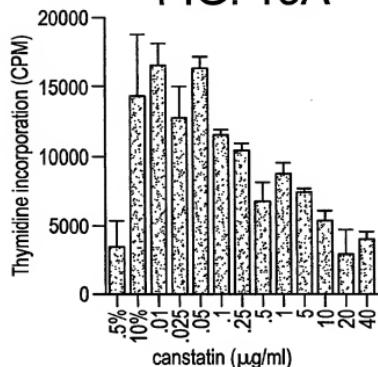


FIG. 13B

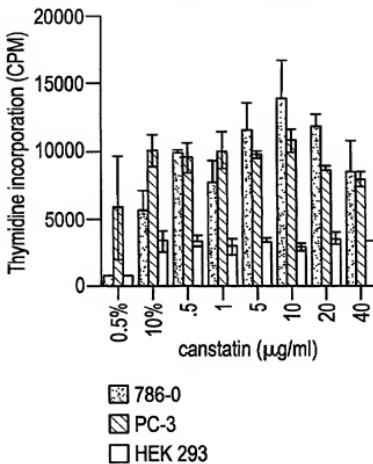


FIG. 13C

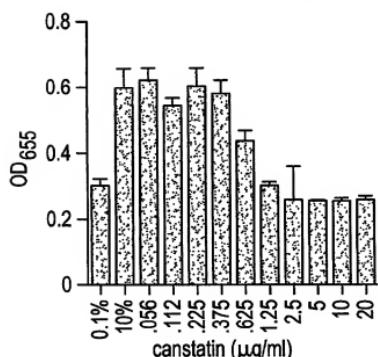


FIG. 13D

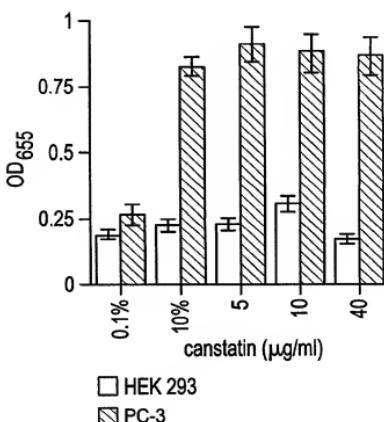


FIG. 14

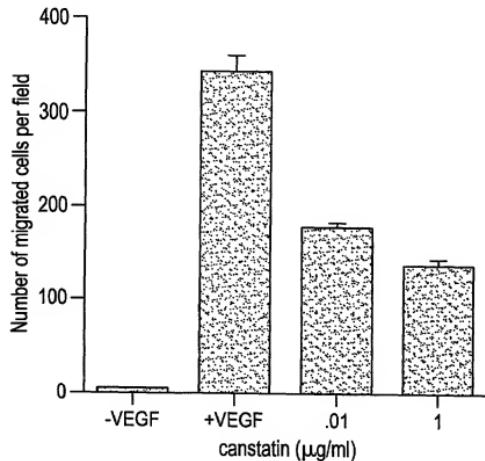
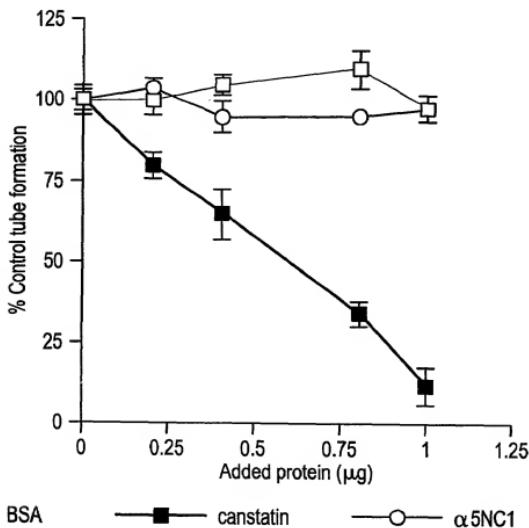


FIG. 15



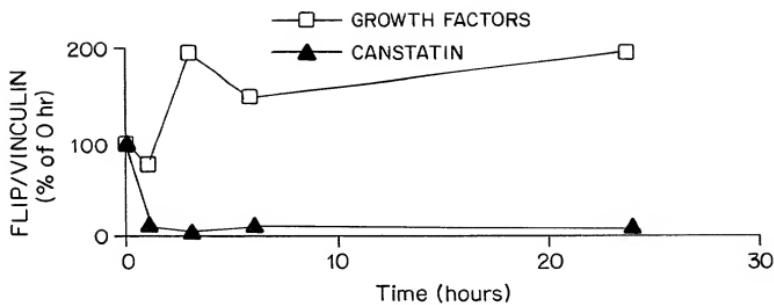


FIG. 16

FIG. 17A

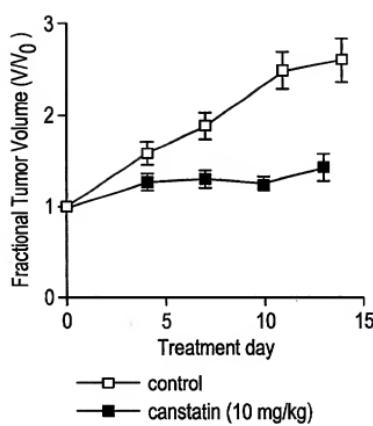


FIG. 17B

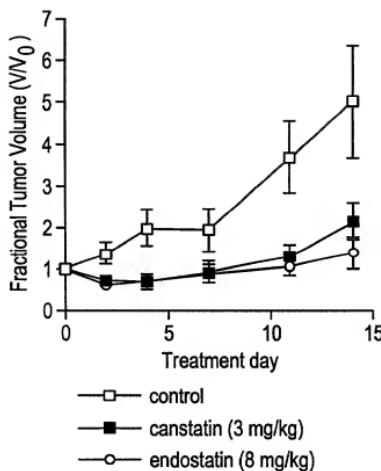


FIG. 17C

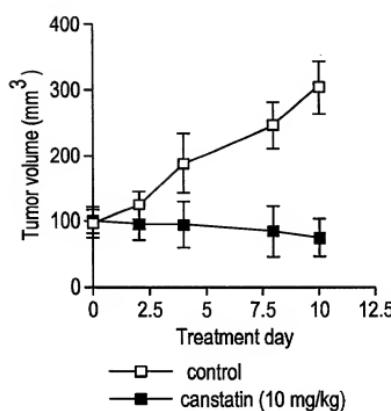


FIG. 17D

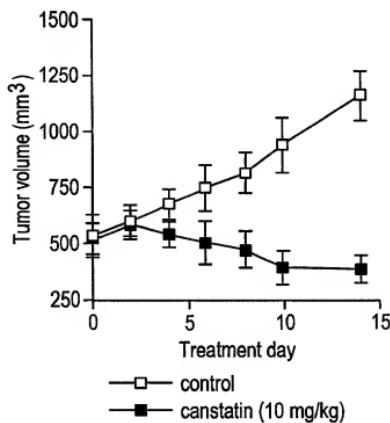


FIG. 18A

pET22b(+) forward primer:

5'-CGGGAT CCA GGT TTG AAA GGA AAA CGT-3' (SEQ ID NO:11)

pET22b(+) reverse primer:

5'-CCCAAGCTT TCA GTG TCT TTT CTT CAT-3' (SEQ ID NO:12)

5	10	15	20	25	30	35	40	45															
cca	ggt	ttg	aaa	qga	aaa	cat	gga	gac	agt	gga	tca	cct	gca	acc									
50	55	60	65	70	75	80	85	90	tgg	aca	acg	aga	ggc	ttt	gtc	ttc	acc	cga	cac	agt	caa	acc	aca
95	100	105	110	115	120	125	130	135	gca	att	cct	tca	tgt	cca	gag	ggg	aca	gtg	cca	ctc	tac	agt	ggg
140	145	150	155	160	165	170	175	180	ttt	tct	ttt	ctt	ttt	gta	caa	gga	aat	caa	cga	gcc	cac	gga	caa
185	190	195	200	205	210	215	220	225	gac	ctt	gga	act	ctt	ggc	agc	tgc	ctg	cag	cga	ttt	acc	aca	atg
230	235	240	245	250	255	260	265	270	cca	ttc	tta	ttc	tgc	aat	gtc	aat	gat	gta	tgt	aat	ttt	gca	tct
275	280	285	290	295	300	305	310	315	cga	aat	gat	tat	tca	tac	tgg	ctg	tca	aca	cca	gct	ctg	atg	cca
320	325	330	335	340	345	350	355	360	atg	aac	atg	gct	ccc	att	act	ggc	aga	gcc	ctt	gag	cct	tat	ata
365	370	375	380	385	390	395	400	405	agc	aga	tgc	act	gtt	tgt	gaa	ggt	cct	gcg	atc	gcc	ata	gcc	gtt
410	415	420	425	430	435	440	445	450	cac	agc	caa	acc	act	gac	att	cct	cca	tgt	cct	cac	ggc	tgg	att
455	460	465	470	475	480	485	490	495	tct	ctc	tgg	aaa	gga	ttt	tca	ttc	atc	atg	ttc	aca	agt	gca	ggt
500	505	510	515	520	525	530	535	540	tct	gag	ggc	acc	ggg	caa	gca	ctg	gcc	tcc	cct	ggc	tcc	tgc	ctg
545	550	555	560	565	570	575	580	585	gaa	gaa	ttc	cga	gcc	agc	cca	ttt	cta	gaa	tgt	cat	gga	aga	gga
590	595	600	605	610	615	620	625	630	acg	tgc	aac	tac	tat	tca	aat	tcc	tac	agt	ttc	tgg	ctg	gct	tca
635	640	645	650	655	660	665	670	675	tta	aac	cca	gaa	aga	atg	ttc	aga	aag	cct	att	cca	tca	act	gtg
680	685	690	695	700	705	710	715	720	aaa	gct	ggg	gaa	tta	gaa	aaa	ata	ata	agt	cgc	tgt	cag	gtg	tgc
725	730	735							atg	aag	aaa	aga	cac	tga									

(SEQ ID NO:9)

pET22b- α 3(IV) NC1 = nucleotides 4 through 735

Tumstatin 333 = nucleotides 4 through 375

Tumstatin 334 - nucleotide 376 through 735

FIG. 18B

* 5 10 15 20 25 30 35 40 45
PGL KGK RGD SGS PAT WTT RGF VFT RHS QTT AIP SCP EGT VPL YSG

50 55 60 65 70 75 80 85 90
FSF LFV QGN QRA HQQ DLG TLG SCL QRF TTM PFL FCN VND VCN FAS

*+ 95 100 105 110 115 120 125 130 135
RND YSY WLS TPA LMP MNM API TGR ALE PYI SRC TVC EGP AIA IAV

140 145 150 155 160 165 170 175 180
HSQ TTD IPP CPH GWI SLW KGF SFI MFT SAG SEG TGQ ALA SPG SCL

185 190 195 200 205 210 215 220 225
EEF RAS PFL ECH GRG TCN YYS NSY SFW LAS LNP ERM FRK PIP STV

+ 230 235 240 245
KAG ELE KII SRC QVC MKK RH (SEQ ID NO:10)

pET22b α 3(IV) NC1 = residues 2 through 245

Tumstatin 333 = residues 2 through 125

Tumstatin 334 = residues 126 through 245

FIG. 19

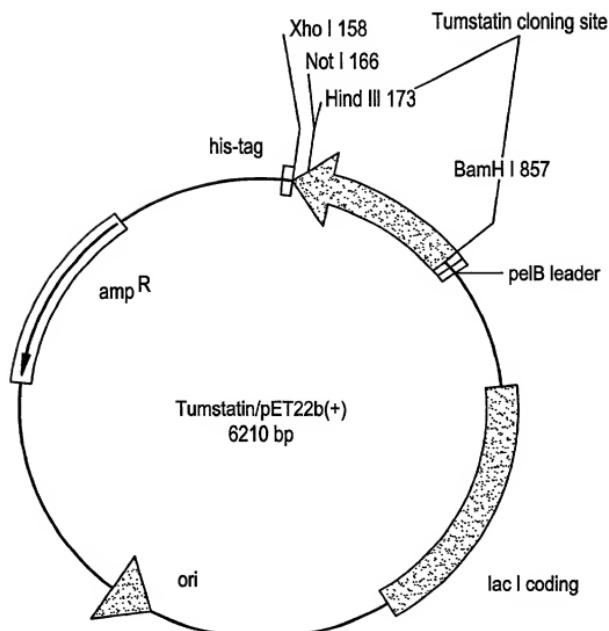


FIG. 20

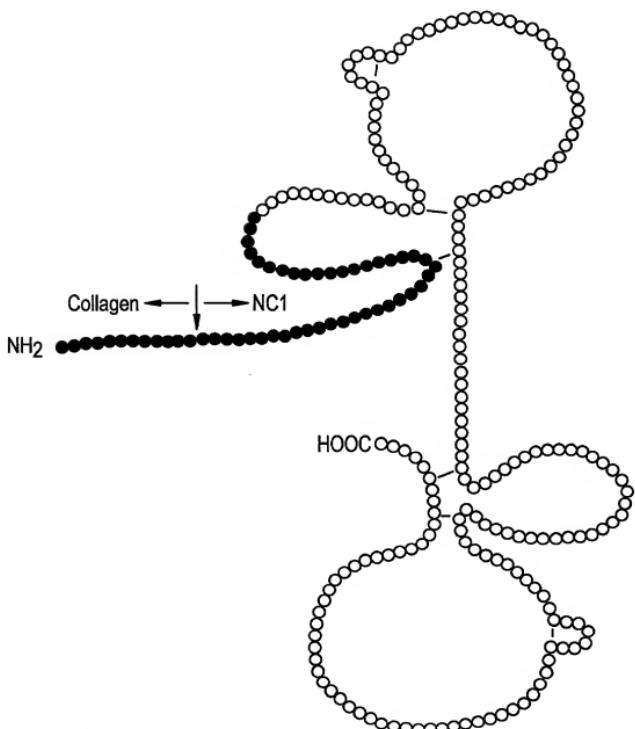


FIG. 21A

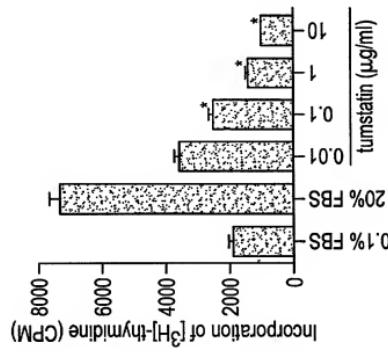


FIG. 21B

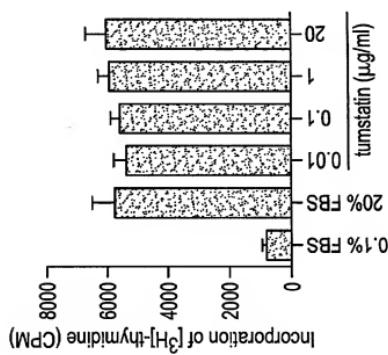
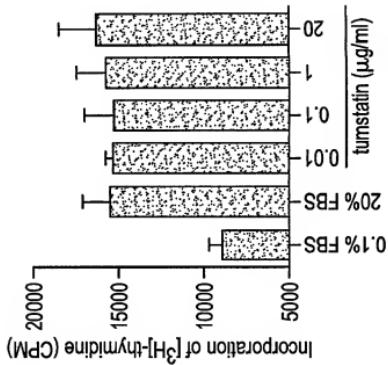


FIG. 21C



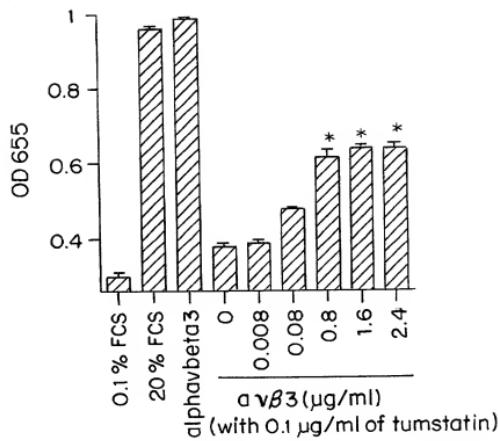


FIG. 22

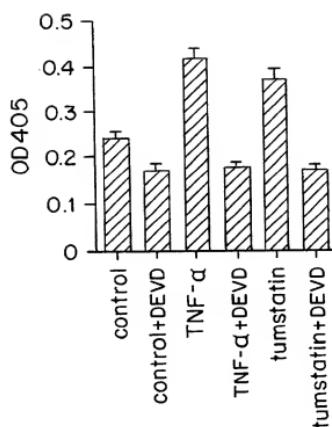


FIG. 23A

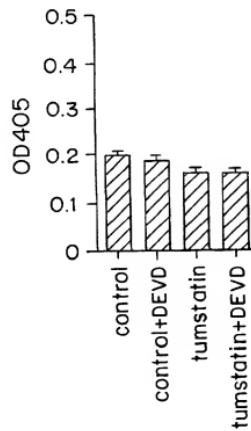


FIG. 23B

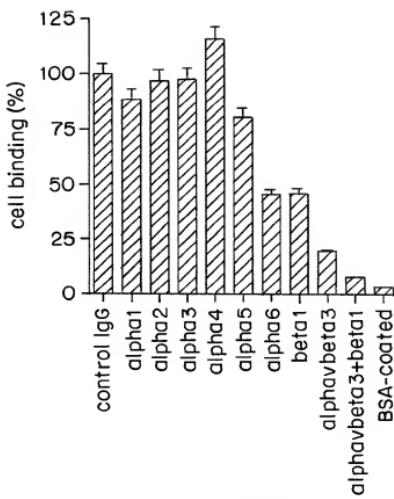


FIG. 24A

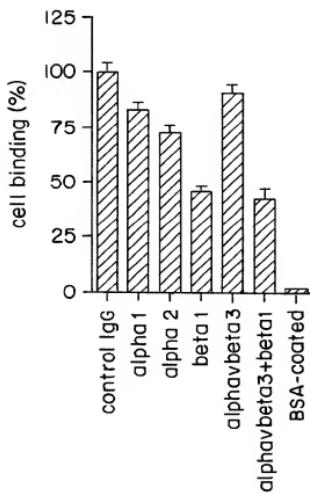


FIG. 24B

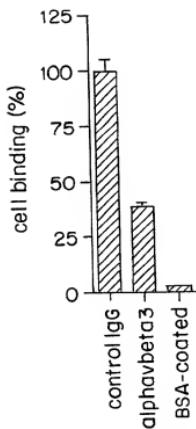


FIG. 24C

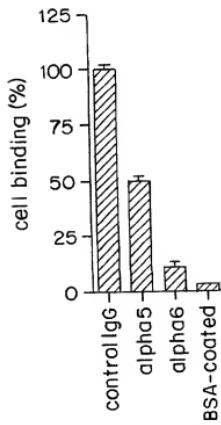


FIG. 24D

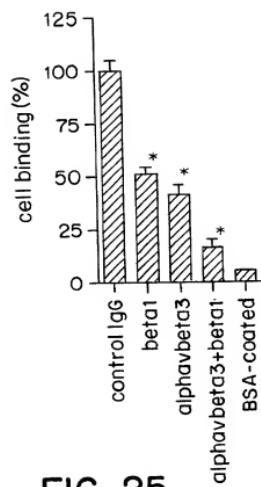


FIG. 25

FIG. 26

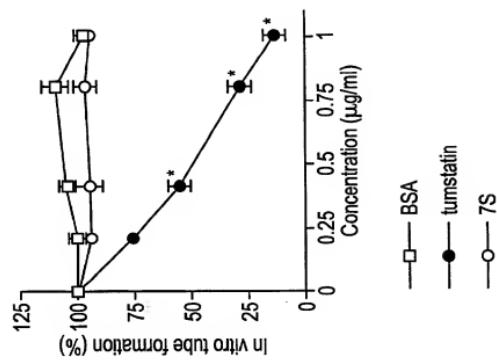


FIG. 27A

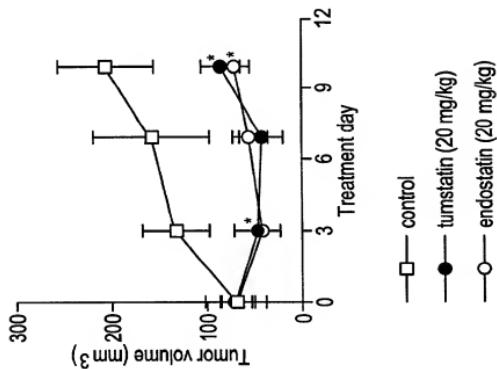


FIG. 27B

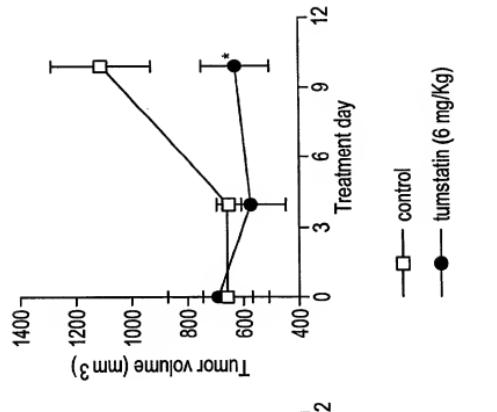
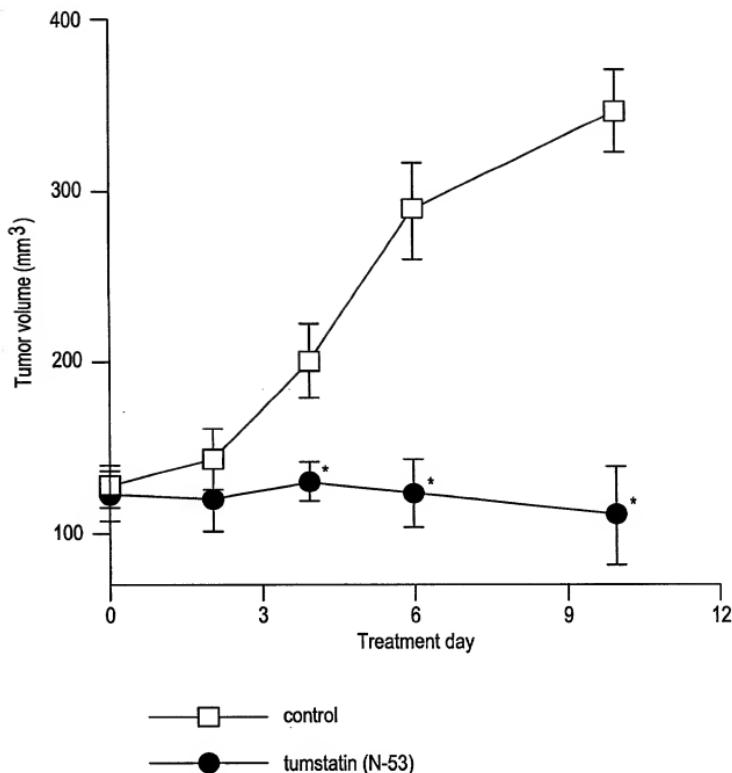


FIG. 28



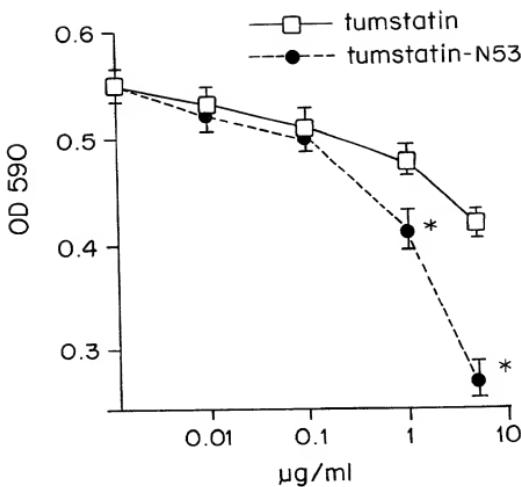


FIG. 29

FIG. 30

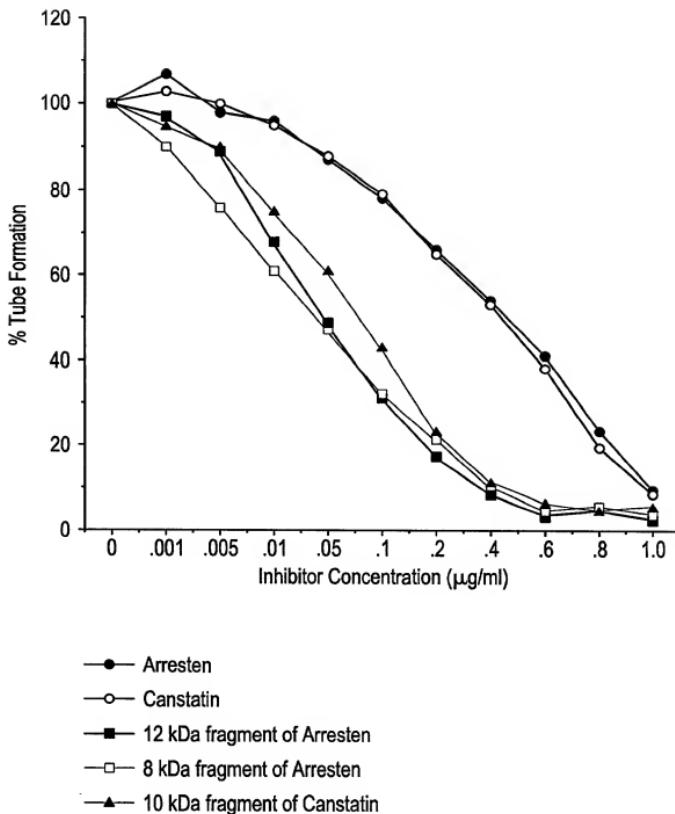
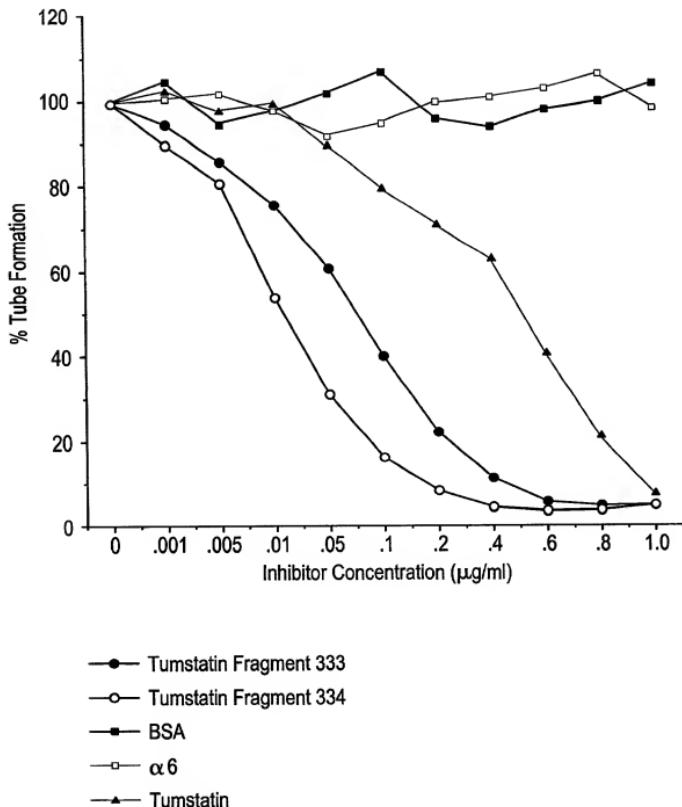


FIG. 31



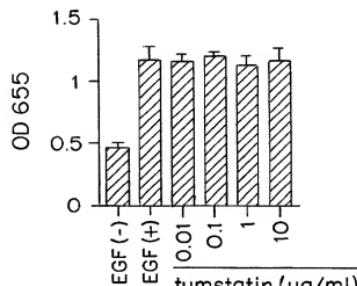


FIG. 32A

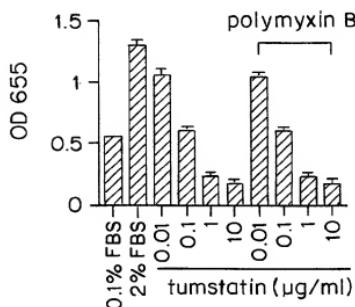


FIG. 32B

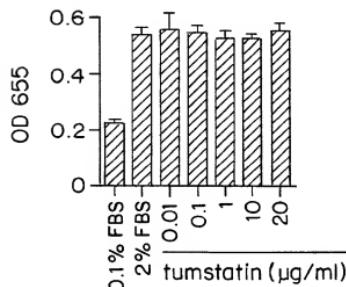


FIG. 32C

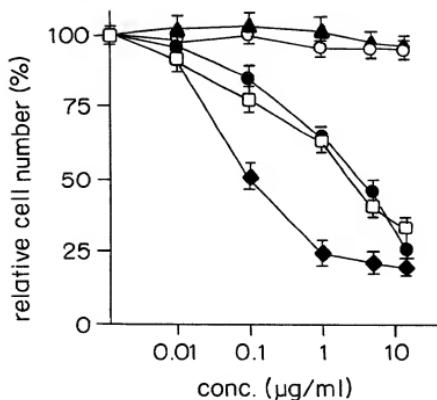


FIG. 33A

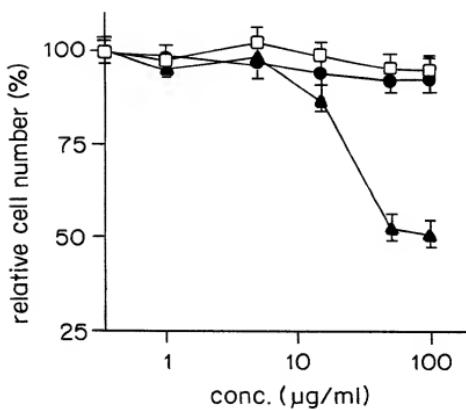


FIG. 33B

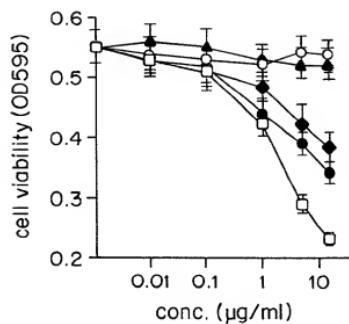


FIG. 34A

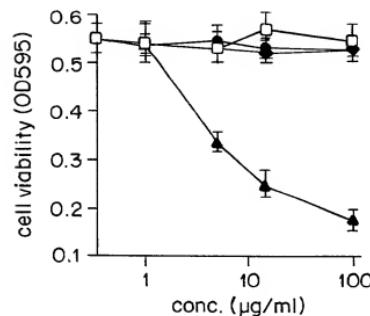


FIG. 34B

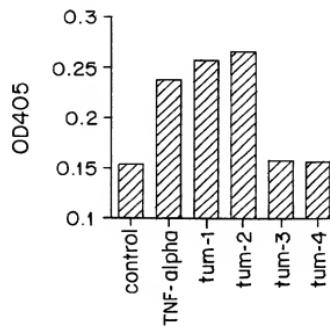


FIG. 35

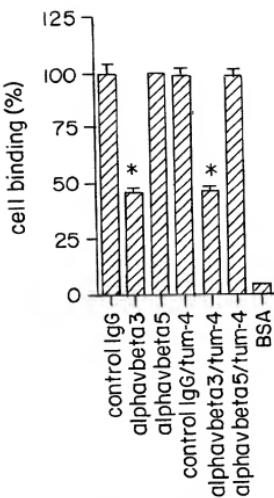


FIG. 36A

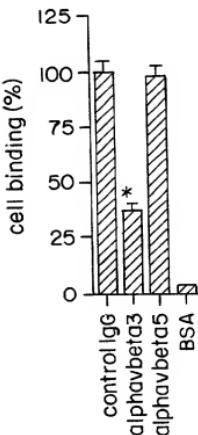


FIG. 36C

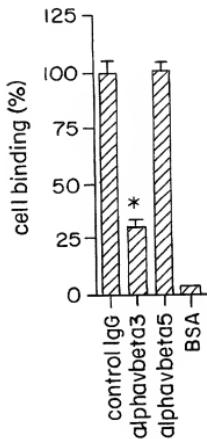


FIG. 36B

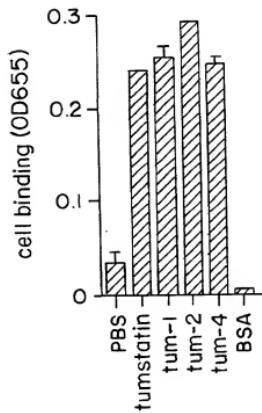


FIG. 37

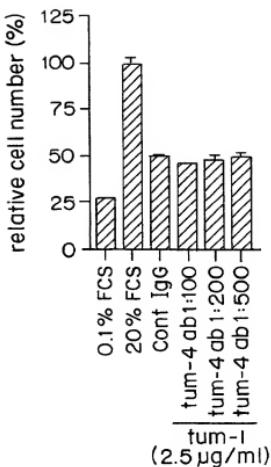


FIG. 38A

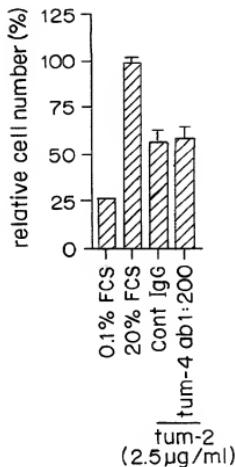


FIG. 38B

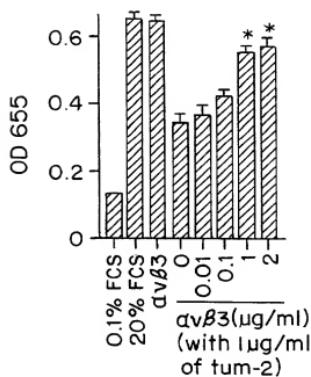


FIG. 38C

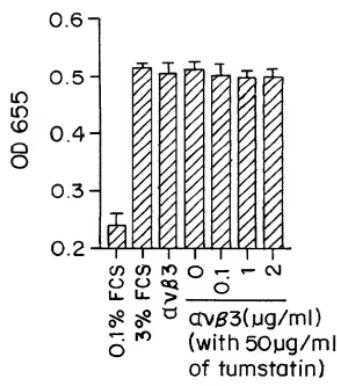


FIG. 38D

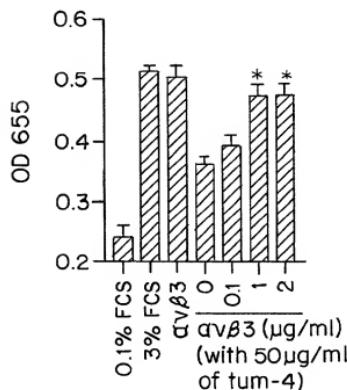


FIG. 38E

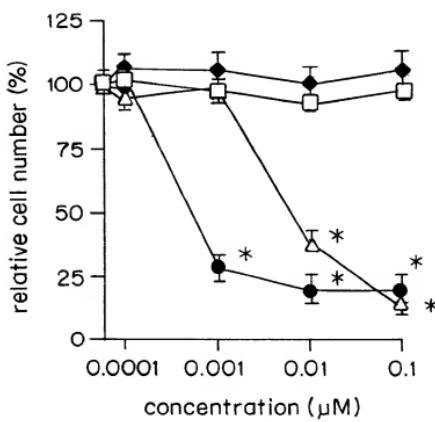


FIG. 39

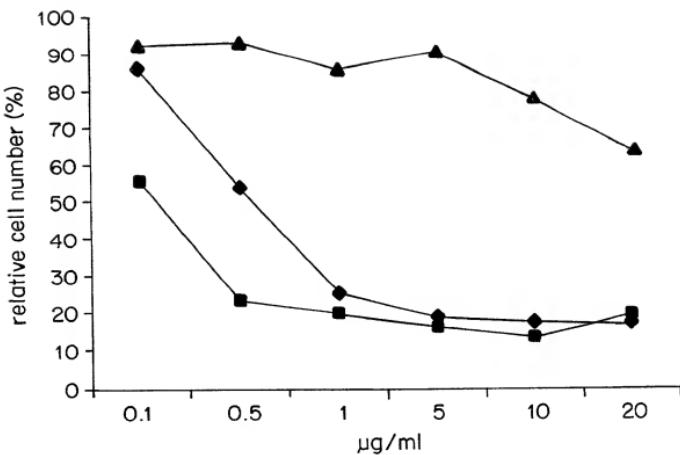


FIG. 40

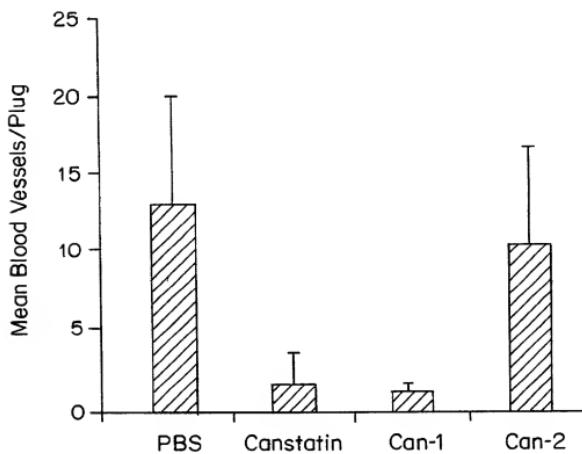


FIG. 41

FIG. 42

T1 GP-A
PGLKGK**RGD**SGSPATWTTTRGFVFTRHSQT**TAIPSCPEGTVPLY**

T2 T3 T4
SGFSFLFVQGNQRAHGQDLGTLGSCLQRFTT**MPFLFCNVNDVC**

T3 T5 T4 T6
T4 T5 T6
NFASRNDYSYWLSTPALMPMNMAPITGRALEPYISRCTVCEGP

T6 GP-B
AIAIAVHSQT**TDIPP**CPHGWI**SLWK**GFSFIMFTSAGSEGTGQA
LASPGSCLEEFRASPFL**ECHGRGT**CNYYSNSYSFWLASLNPER
MFRKPIPSTVKAGELEKI**ISRCQVCMKKR**H

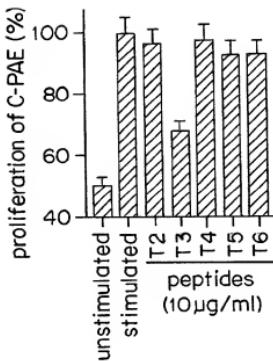


FIG. 43A

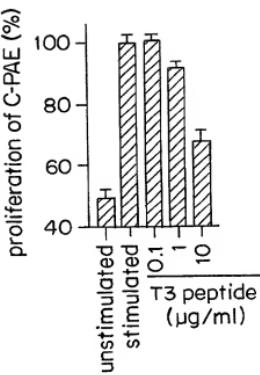


FIG. 43B

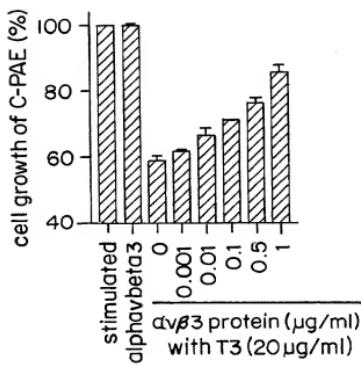


FIG. 43C

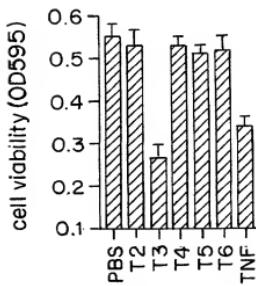


FIG. 43D

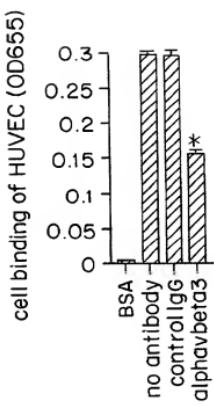


FIG. 44A

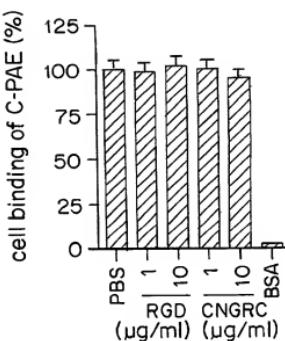


FIG. 44B

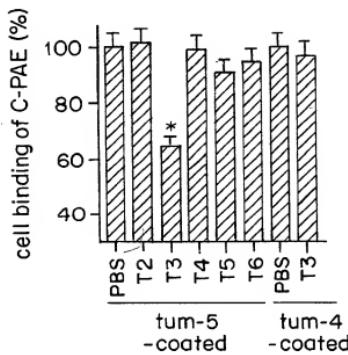


FIG. 44C

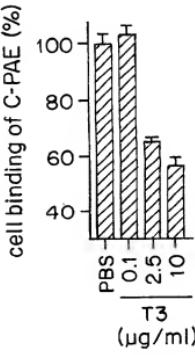


FIG. 44D

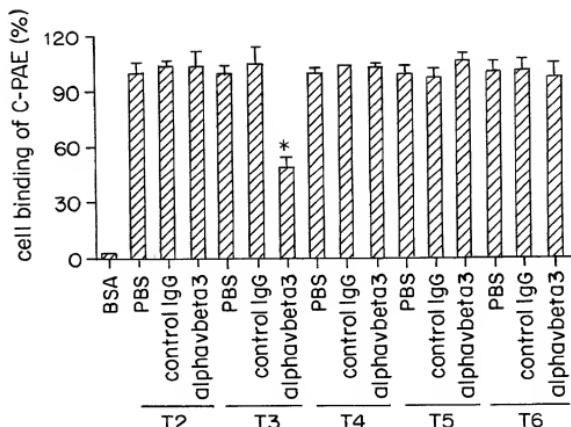


FIG. 44E

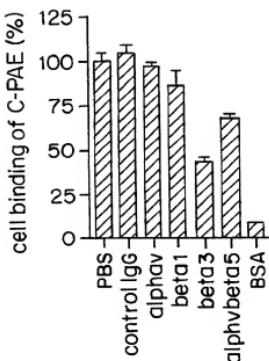


FIG. 44F

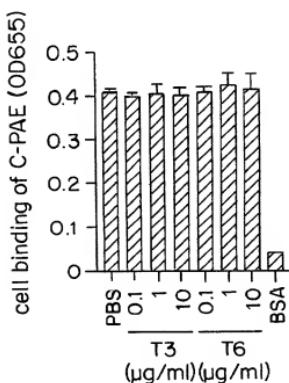


FIG. 44G

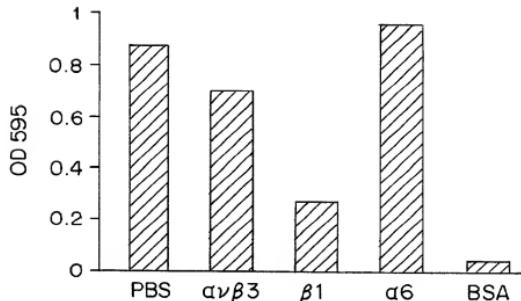


FIG. 45

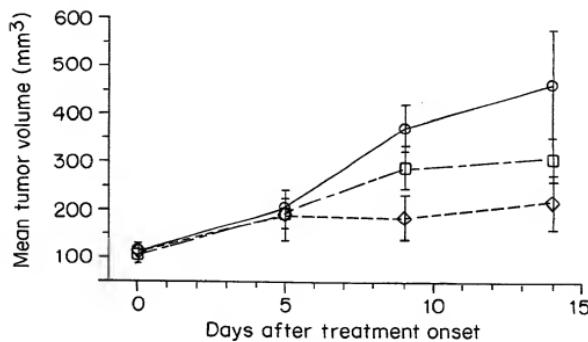


FIG. 46

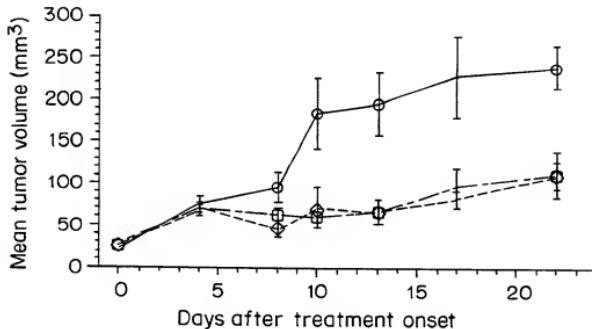


FIG. 47

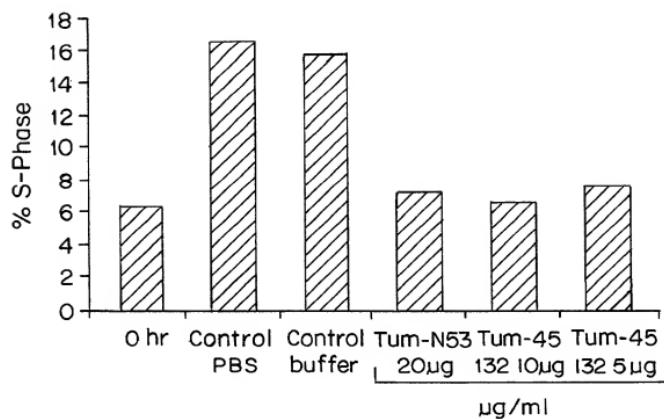


FIG. 48

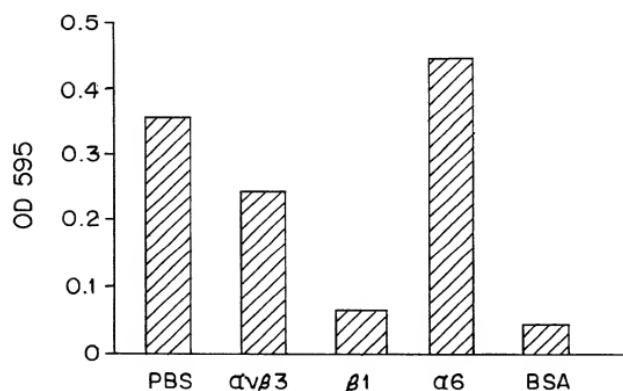


FIG. 49

Fig. 50

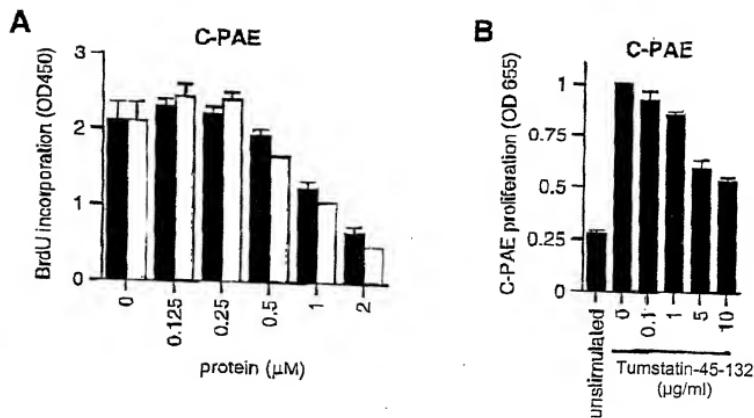


Fig. 51

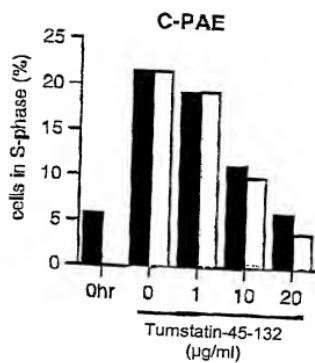


Fig. 52

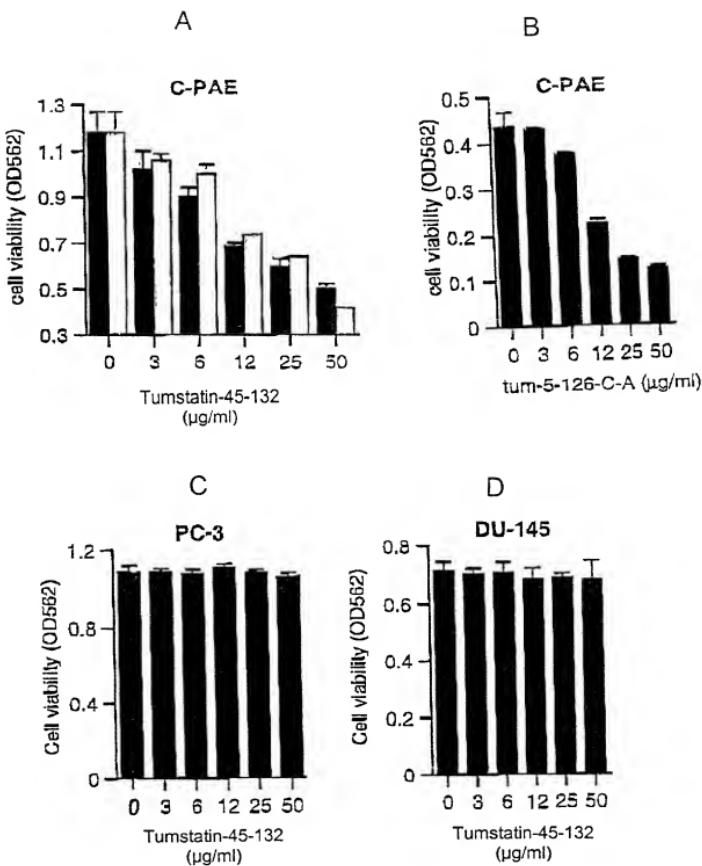


Fig. 54

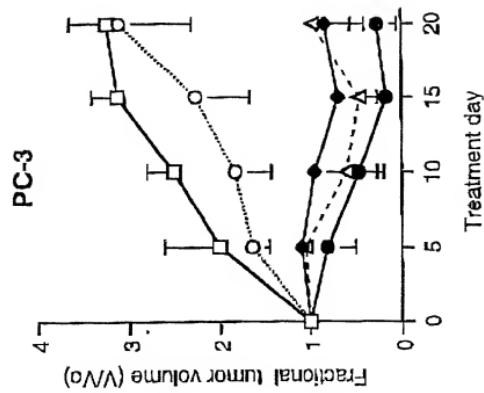
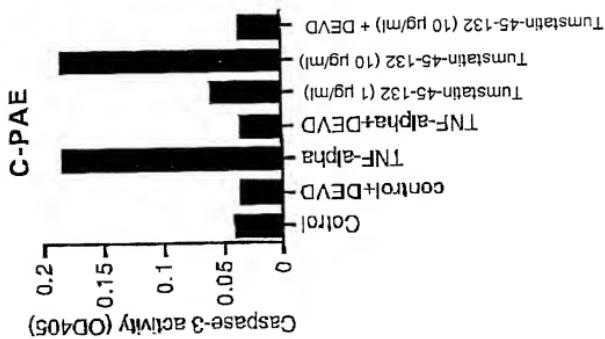


Fig. 53



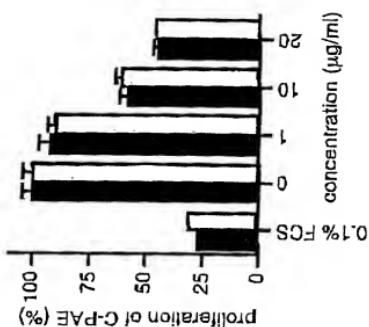


Fig.
56

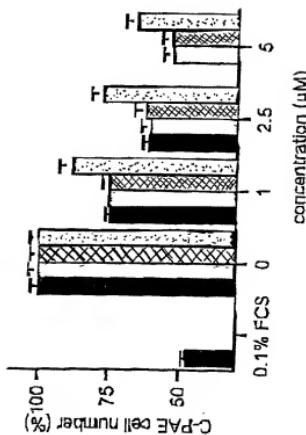


Fig.
57

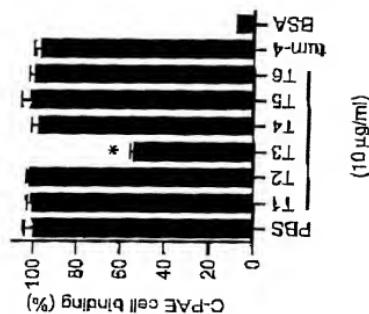


Fig.
55A



Fig.
55B

Fig. 58A

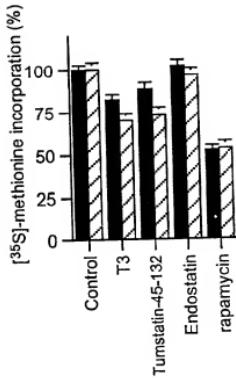


Fig. 58B

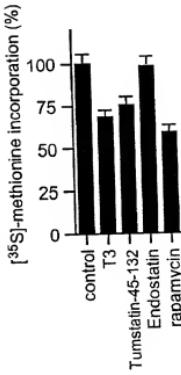


Fig. 58C

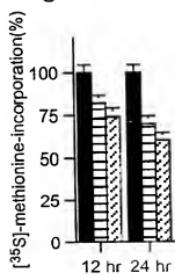


Fig. 58D

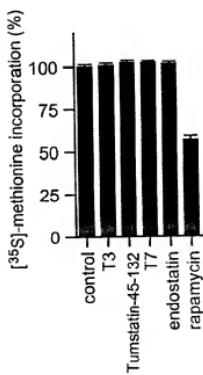


Fig. 58E

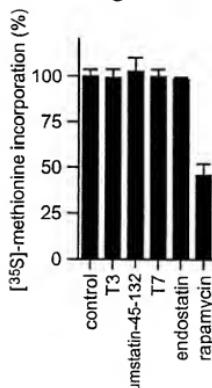


Fig. 58F

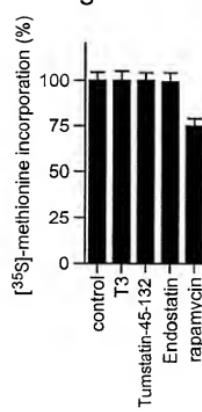


Fig. 58G

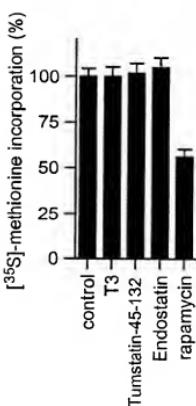


Fig. 58H

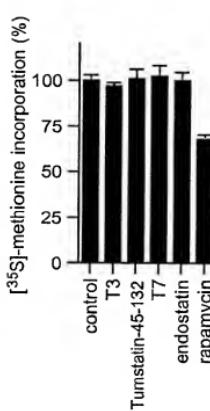


Fig. 59A

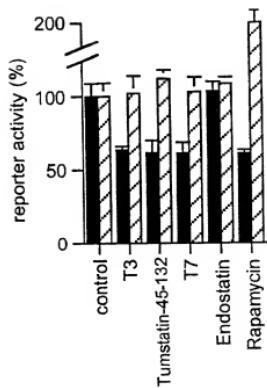


Fig. 59B

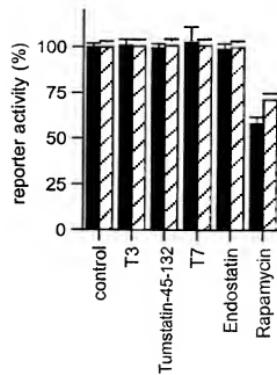


Fig. 60A

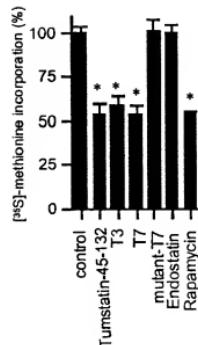


Fig. 60B

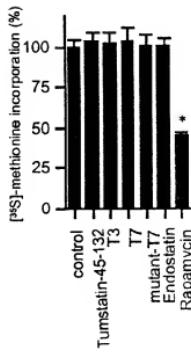


Fig. 60C

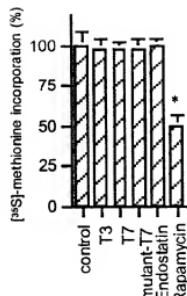


Fig. 60D

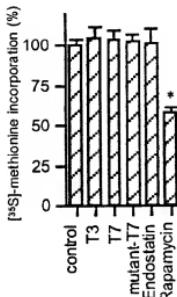


Fig. 60E

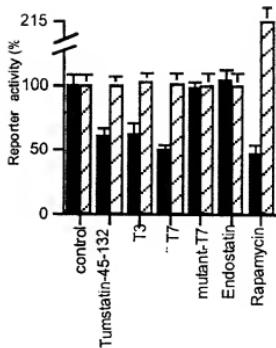


Fig. 60F

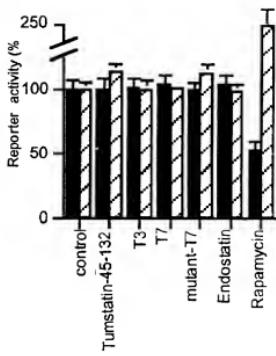


Fig. 60G

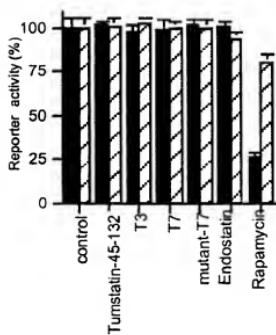


Fig. 60H

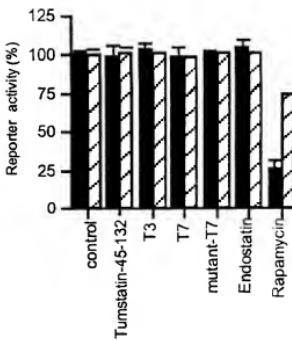


Fig. 61A

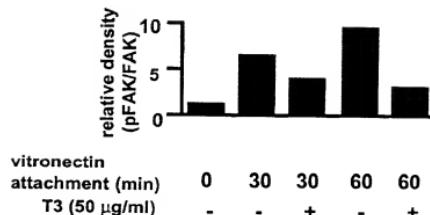


Fig. 61B

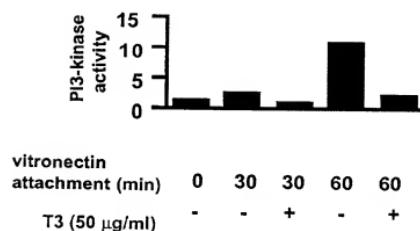


Fig. 61C

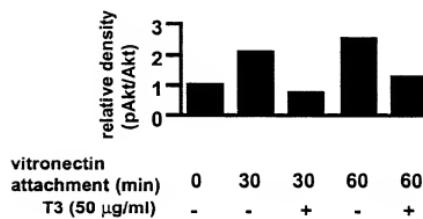


Fig. 61D

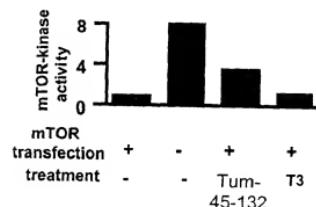


Fig. 61E

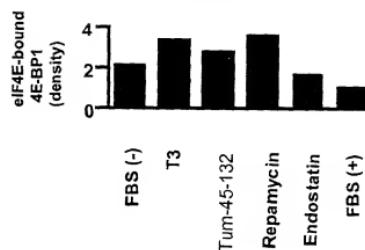
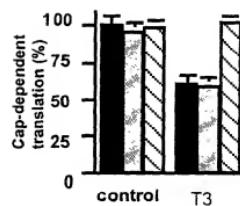


Fig. 61F



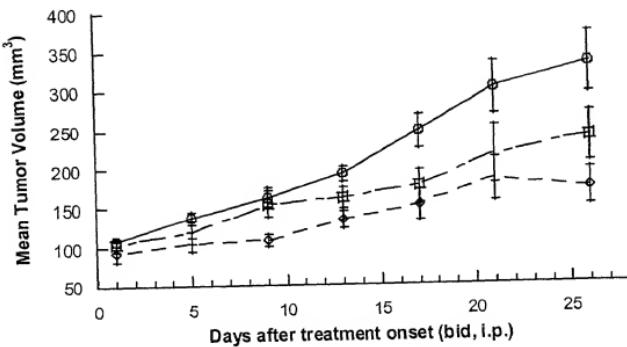


Fig. 62

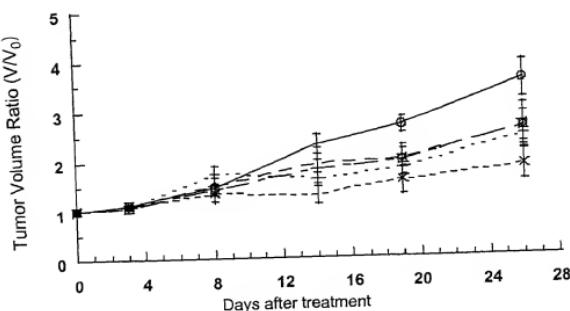


Fig. 63

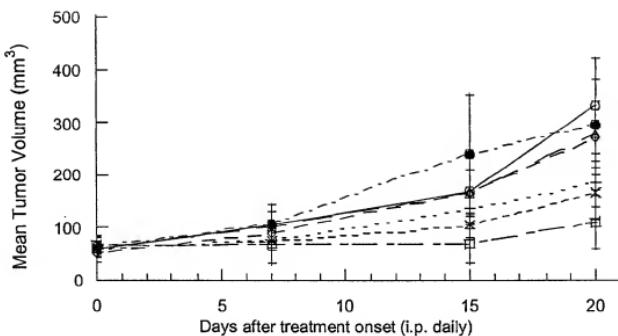


Fig. 64A

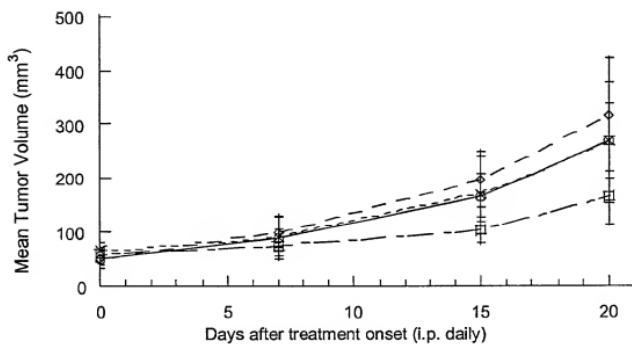


Fig. 64B

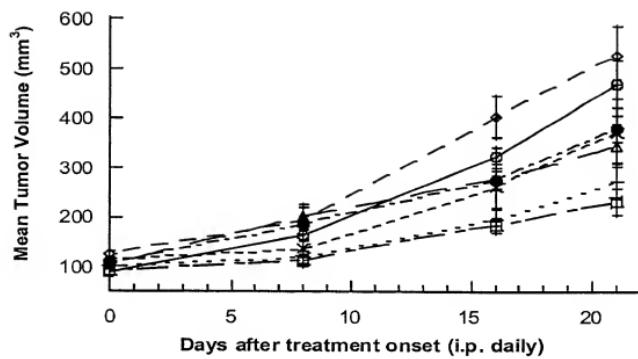


Fig. 65A

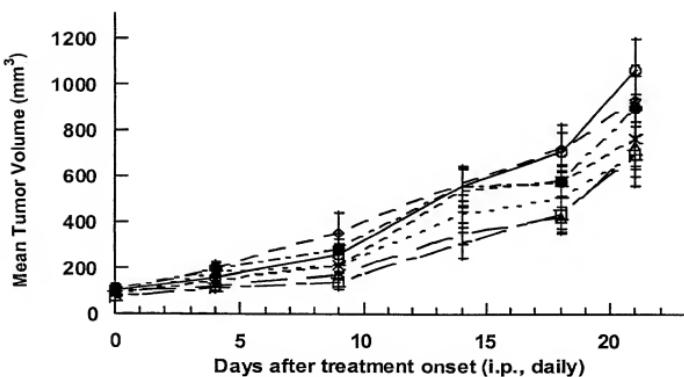


Fig. 65B